Common Drug Review

Pharmacoeconomic Review Report

January 2014

Drug	somatropin (Genotropin) for subcutaneous injection
Indication	Long-term treatment of children who have growth failure due to an inadequate secretion of endogenous growth hormone
Listing request	List in a similar manner to other growth hormone products
Manufacturer	Pfizer Canada Inc.

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The report contains an evidence-based clinical and/or pharmacoeconomic drug review, based on published and unpublished material, including manufacturer submissions; studies identified through independent, systematic literature searches; and patient-group submissions. In accordance with *CDR Update — Issue 87*, manufacturers may request that confidential information be redacted from the CDR Clinical and Pharmacoeconomic Review Reports.

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ABBREVIATIONS

CDR	Common Drug Review
GHD	growth hormone deficiency

SUMMARY

Somatropin (Genotropin) is available as an injection with multiple strengths (0.6 mg, 0.8 mg, 1.0 mg, 1.2 mg, 1.4 mg, 1.6 mg, 1.8 mg, and 2.0 mg syringes, and 5.3 mg and 12 mg pens). It is indicated in Canada for the treatment of children who have growth failure due to an inadequate secretion of endogenous growth hormone (growth hormone deficiency), growth failure in short children born small for gestational age who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome in patients whose epiphyses are not closed, idiopathic short stature, and adults with growth hormone deficiency of adult or childhood-onset. The manufacturer is requesting listing for reimbursement for its use in pediatric patients with GHD. Similar clinical effectiveness for Genotropin versus comparators was assumed based on the results of one trial comparing Genotropin with Omnitrope.1 There were no published indirect comparisons of these agents. Based on Common Drug Review calculations using a confidential price of $[redacted] per milligram, the daily cost of the maximum dose of Genotropin ($[redacted]; 0.16 mg/kg to 0.24 mg/kg per week) is less than that of Humatrope ($77; 0.18 mg/kg to 0.30 mg/kg per week), Nutropin ($64; up to 0.30 mg/kg per week), Saizen ($59; 0.20 mg/kg to 0.27 mg/kg per week), and Omnitrope ($42; 0.18 mg/kg to 0.25 mg/kg per week).

REVIEW OF THE PHARMACOECONOMIC SUBMISSION

1. INTRODUCTION

Somatropin (Genotropin) is an injectable recombinant human growth hormone indicated in Canada for the treatment of children who have growth failure due to an inadequate secretion of endogenous growth hormone (growth hormone deficiency; GHD), growth failure in short children born small for gestational age and who fail to achieve catch-up growth by two to four years or later, short stature associated with Turner syndrome in patients whose epiphyses are not closed, idiopathic short stature, and adults with GHD of adult or childhood-onset. This report will review its use in pediatric patients with GHD. The recommended dose of Genotropin in pediatric patients is 0.03 mg/kg per day up to a maximum of 0.034 mg/kg per day. The manufacturer submitted a confidential price of $[redacted] per mg.

1.1 Cost Comparison Table

The comparator treatments presented in the table below have been deemed the appropriate comparators by clinical experts. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

TABLE 1: COST COMPARISON TABLE FOR GENOTROPIN FOR PEDIATRIC GROWTH HORMONE DEFICIENCY

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost[a] ($)	Average Annual Drug Cost ($)
Genotropin[b]	**5.3 mg 12 mg**	**Pen**	[redacted]	**0.16 mg/kg to 0.24 mg/kg body weight per week in 6 to 7 doses**	[redacted] – [redacted]	[redacted] - [redacted]
	0.6 mg 0.8 mg 1.0 mg 1.2 mg 1.4 mg 1.6 mg 1.8 mg 2.0 mg	**Syringe**	[redacted]		[redacted] – [redacted]	[redacted] – [redacted]
Humatrope	5 mg 24 mg	Vial	233.35 999.99	0.18 mg/kg to 0.30 mg/kg body weight per week in 3 to 7 doses	41 to 77	14,985 to 27,976
	6 mg 12 mg	Cartridge	280.02 560.04		46 to 77	16,785 to 27,976
Nutropin	10 mg	Vial	389.44	Up to 0.3 mg/kg per week in divided daily doses	Up to 64	Up to 23,344
Nutropin AQ	10 mg	Cartridge	392.55		Up to 64	Up to 23,530
Omnitrope	5 mg 10 mg	Vial	155.80 311.60	(0.18 to 0.25 mg/kg per week)	30 to 42	10,896 to 15,254

Drug/ Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost[a] ($)	Average Annual Drug Cost ($)
Saizen	3.33 mg 5 mg 8.8 mg	Vial	149.25 224.05 358.47	0.2 to 0.27 mg/kg per week in 3 to 7 doses	45 to 59	16,279 to 24,493
	6 mg 12 mg 20 mg	Cartridge	268.83 537.66 896.10		49 to 59	17,905 to 24,486

Prices are from the Saskatchewan Formulary (accessed Aug 23, 2013) unless otherwise indicated and do not include dispensing fees.
[a] Weight-based doses use an average weight of 38.32 kg as reported in Takeda et al.[1] for pediatric patients with GHD who were between ages 9 and 16. Assumes daily doses and wastage of excess for single-dose syringes.
[b] Manufacturer's confidential submitted price.

2. SUMMARY OF PHARMACOECONOMIC SUBMISSION

The manufacturer submitted a cost-minimization analysis[2] comparing Genotropin to the other somatropin products available in Canada: Humatrope, Saizen, Nutropin, and Omnitrope. Norditropin, an additional somatropin available in Canada, was not included in the analysis since the manufacturer was unable to identify any use of this product in both public and private drug plans across the country. Serostim, another somatropin, was not included as its sole indication in Canada is for treatment of HIV wasting associated with catabolism, weight loss, or cachexia.

Similar clinical effectiveness of Genotropin with comparators was assumed by the manufacturer based on the results of one trial comparing Genotropin to Omnitrope for treatment of GHD in children,[3] the results of which suggest that there is similar efficacy among the different somatropin products (Table 2). No indirect comparisons were identified in the literature search. The analysis was conducted from the Canadian public-payer perspective.

TABLE 2: TRIAL RESULTS FOR OMNITROPE VERSUS GENOTROPIN

	Omnitrope	Genotropin	95% CI
Number of patients	44	45	
Height baseline, cm	113.3	109.3	
Height at 9 months, cm	121.9	117.7	–0.59 to 1.06

CI = confidence interval.
Source: Genotropin Manufacturer Pharmacoeconomic Submission (Table 1, page 16).[2]

Only drug acquisition costs of Genotropin were considered, and these were obtained from the IMS Delta PA database.[2] The manufacturer assumed similar health care resource utilization among all somatropin products. For the drug costs, the manufacturer used the lowest cost per milligram for each product, regardless of the variation in drug formulation or administration system. For the base-case analysis, the adult daily dosage of the products was compared based on the minimum and maximum dosage reported in each comparator's respective product monograph (Table 3). The manufacturer reported that the average daily cost of the maximum dose of Genotropin ($[redacted]) is lower than that of Humatrope ($68), Nutropin ($64), Saizen ($58), and [redacted] Omnitrope ($37). Therefore, at maximum doses, Genotropin would be cost-saving in comparison with Humatrope, Nutropin, Omnitrope, and Saizen (Table 3).

TABLE 3: COST COMPARISON BASED ON MAXIMUM DOSES FOR THE TREATMENT OF PEDIATRIC GROWTH HORMONE DEFICIENCY

Product	Genotropin	Humatrope	Nutropin	Saizen	Omnitrope
Maximum dose (mg/kg per day)[a]	0.034	0.043	0.043	0.039	0.035
Daily cost	$[redacted]	$67.97	$63.94	$58.45	$37.42
Annual cost	$[redacted]	$24,808.16	$23,339.69	$21,334.78	$13,656.77
Incremental annual cost (savings) compared with Genotropin		**$11,430**	**$9,962**	**$7,957**	**$[redacted]**

Adapted from Genotropin Manufacturer Pharmacoeconomic Submission (Tables 3 and 7, pages 19 and 22).[2]
[a] Dosages for Humatrope, Saizen, and Nutropin are based on an average pediatric weight of 38.32 kg.[1]

The manufacturer conducted a sensitivity analysis using a dose of 0.025 mg/kg per day as the treatment for pediatric patients with GHD. This dose is based on the clinical study by Takeda et al.[1] The results suggested that the annual cost of Genotropin is lower than that of Humatrope, Nutropin, and Saizen, and [redacted] that of Omnitrope (Table 4).

TABLE 4: MANUFACTURER-SUBMITTED SENSITIVITY ANALYSIS RESULTS FOR THE TREATMENT OF PEDIATRIC GROWTH HORMONE DEFICIENCY

Product	Genotropin	Humatrope	Nutropin	Saizen	Omnitrope
Average annual cost per patient[a]					
	$[redacted]	$14,471	$13,615	$13,828	$9,755

[a] Based on the mean daily dose (0.025 mg/kg per day) in the analysis by Takeda et al. 2010.

3. INTERPRETATIONS AND KEY LIMITATIONS

3.1 Lack of evidence to support equivalent efficacy and safety

Equivalent efficacy was assumed based on a single head-to-head trial comparing Genotropin to Omnitrope in pediatric patients with GHD.[3] No indirect comparisons were identified in a literature search carried out by Common Drug Review (CDR).

4. ISSUES FOR CONSIDERATION

The manufacturer is requesting that Genotropin be listed for use in pediatric patients with GHD. Somatropin, available through other brand names and products, is indicated for additional conditions such as idiopathic short stature, short stature homeobox-containing gene deficiency, small for gestational age, and in children with growth failure due to chronic renal failure. The potential for off-label use of Genotropin can be associated with considerable costs to the drug plans. However, it should be noted that the possibility of off-label use is not unique to Genotropin and applies to the other available somatropin products on the market in Canada.

A CDR analysis of potential utilization in pediatric GHD patients in Canada (see APPENDIX 1: UTILIZATION ANALYSIS) suggested that Genotropin could be associated with cost savings of up to $216,529 per year for public plans.

5. CONCLUSIONS

Based on CDR calculations using a confidential price of $[redacted] per milligram, the daily cost of the maximum dose of Genotropin ($[redacted]; 0.16 mg/kg to 0.24 mg/kg per week) is less than that of Humatrope ($77; 0.18 mg/kg to 0.30 mg/kg per week), Nutropin ($64; up to 0.3 mg/kg per week), Saizen ($59; 0.20 mg/kg to 0.27 mg/kg per week), and Omnitrope ($42; 0.18 mg/kg to 0.25 mg/kg per week).

APPENDIX 1: UTILIZATION ANALYSIS

The submitted price for Genotropin ($[redacted] per milligram) is lower than that of Humatrope ($41.39 per milligram), which is the most widely reimbursed somatropin in Canada (based on public plan data), with an approximate market share of 58% in 2012. A scenario analysis was conducted in which Genotropin was assumed to replace Humatrope. Based on available prevalence data[4,5] and Canadian population estimates by age and gender for 2012,[6] this scenario analysis assumed that 12.93% of all units reimbursed for Humatrope were used by pediatric patients with GHD. This analysis is based on public coverage of Humatrope (no private plans are included). For product costs, both available provincial drug prices and manufacturer-submitted average prices per milligram were used. The results in Table 5 indicate the potential annual cost savings to the drug plan if Genotropin replaced Humatrope.

TABLE 5: CDR ANALYSIS OF UTILIZATION FOR GENOTROPIN

Current Price[a] ($/mg)	Scenario	Minimum Savings[b]	Maximum Savings[b]
$[redacted]	Genotropin replaces the most widely used somatropin (Humatrope)[c,d]	$151,460	$216,529

[a] Manufacturer-submitted confidential price.
[b] Savings per year based on provincial and manufacturer-submitted drug prices.
[c] Based on somatropin comparator with most units covered by Canadian public drug plans in 2012, IMS Brogan PharmaStat.
[d] Assumes that 12.93% of patients receiving Humatrope were pediatric patients with GHD.

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